Randomised trial comparing completeness of adjuvant chemotherapy after vs. late diverting stoma closure in low anterior resection for rectal cancer (COCSTOM – TRIAL)

1. STUDY SYNOPSIS

APPLICANT/COORDINATING INVESTIGATOR	Prof. Peter. Kienle, MD, Professor of the University Medical Centre Mannheim, Medical Faculty Mannheim, University of Heidelberg, Germany born 23.08.1966, nationality: German Surgical Department, University Medical Centre Mannheim, Medical Faculty Mannheim, University of Heidelberg, Theodor-Kutzer-Ufer 1-3, D-68167 Mannheim, Tel: +49/621/383-2907; Fax: +49/621/383-2166 email: peter.kienle@umm.de Andreas-Hofer-Weg 55, 69121 Heidelberg, Tel.: 06221-400783, Handy: 01607010450
TITLE OF STUDY	Randomised trial comparing completeness of adjuvant chemotherapy after early vs. late diverting stoma closure in low anterior resection for rectal cancer
CONDITION	Closure of diverting stoma
OBJECTIVE(S)	To investigate **C**ompleteness **o**f adjuvant **C**hemotherapy (CoC) and quality of life (QoL), morbidity and disease free survival after early versus late diverting **stoma** closure
INTERVENTION(S)	Experimental intervention: Early stoma closure 4 weeks after tumor resection followed by chemotherapy starting within 8 weeks after tumor resection Control intervention: Late stoma closure after completion of adjuvant chemotherapy 24 weeks after tumor resection Follow-up per patient: 6 and 24 months after randomization Duration of intervention per patient: Surgical procedure: 30 to 120 min. for closure of diverting stoma Experimental and / or control off label or on label in Germany: not applicable
KEY INCLUSION AND EXCLUSION CRITERIA	Key inclusion criteria: elective curative low anterior resection (LAR) with total mesorectal excision (TME) and diverting stoma after neoadjuvant chemoradiation for UICC II – III rectal cancer, no anastomotic leakage after LAR, indication for adjuvant chemotherapy, written informed consent, age>18 years, patients are able to cooperate Key exclusion criteria: ASA > 3, inflammatory bowel disease, contraindication to adjuvant chemotherapy arising after rectal cancer resection, immunocompromised patients
OUTCOME(S)	Primary efficacy endpoint: Completeness of adjuvant Chemotherapy (CoC) defined as the percentage of randomized patients which complete all planned cycles of adjuvant chemotherapy Key secondary endpoint(s): QoL (EORTC QLQ-C30, CR 29), stoma-related complications, individual CoC rate calculated for each patient, percentage of patients receiving dose modifications or delay, disease-free survival, local recurrence-free survival and distant recurrence-free survival, cumulative days of hospitalisation and number of readmissions, rate of symptomatic anastomotic leaks after stoma closure, mortality, post-op complications Clavien-Grade 4 Assessment of safety: Specification of adverse and serious adverse events.
STUDY TYPE	Randomized, controlled, two parallel group, multicenter trial

STATISTICAL ANALYSIS	Efficacy / test accuracy: Confirmatory analysis for primary outcome, descriptive analysis of secondary outcomes. Description of the primary efficacy / test accuracy analysis and population: The analysis is based on the intention-to-treat population using the ITT principles (dropouts and missings will be counted as failures). For the analysis of the primary endpoint, completeness of chemotherapy, an unconditional exact test will be used. Corresponding 95% confidence intervals will be calculated for the CoC rates in both groups and for the rate difference and odds ratio. There will be stratification by centre. Safety: Calculation and descriptive comparison of the rates of adverse and serious adverse events based on all included patient. Secondary endpoints: Exploratory analysis of quality of life, individual CoC rate, percentage of patients receiving dose modification or delay, disease-free survival, local recurrence-free survival and distant recurrence-free survival,, length of hospitalisation, number of readmissions, number of stoma-related complications and re-operations, rate of symptomatic anastomotic leakages
SAMPLE SIZE	To be assessed for eligibility: **(n = 400)** To be allocated to trial: **(n = 257)** To be analysed: **(n = 214)**
TRIAL DURATION	First patient in to last patient out (months): Jan 2012 - Dec 2014 (36 months) Duration of the entire trial (months): Oct 2011 - Jun 2015 (42 months) Recruitment period (months): Jan 2012 – Dec 2012 (12 months)
PARTICIPATING CENTERS	To be involved (n): **30** Signed agreement to participate (n): **39** The centres marked with * confirmed their participation per fax. The original agreements will be sent to DFG as soon as they will reach UMM.
PREVIOUS DFG / BMBF PROJECT NUMBER	Not applicable